REMARKS

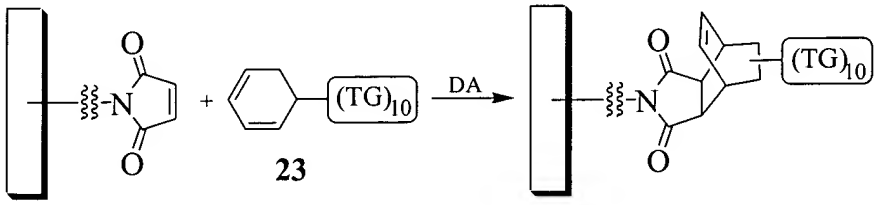
In response to the Office Action of November 26, 2004, claims 32-41 are canceled. Applicant notes that under the section entitled "Disposition of Claims" on page 1 of the Office Action, claims 1-3, 8, 11-18 and 23-41 are listed as the claims currently pending in the instant application. Applicant believes, however, that claim 21 which is not listed is still pending in the application. Claims 1-3, 8, 13-15, 17, 18, 23 and 24 were rejected under 35 U.S.C. § 102(b) as being anticipated by Keana *et al.*, U.S. Pat. No. 5,580,697. Claims 11, 12 and 16 were objected to as being dependent on a rejected claim and claims 25-31 were allowed. Newly submitted claims 32-41 were withdrawn from consideration as being directed to a non-elected invention. Claim 21 was neither rejected, objected to, allowed or withdrawn from consideration by the Examiner, and should be considered as pending in this application. The rejection raised by the Examiner is discussed below.

The Court of Appeals for the Federal Circuit has stated that anticipation requires the presence in a single prior art reference of each and every element of the claimed invention. Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1458 (Fed. Cir. 1984); Alco Standard Corp. v. Tennessee Valley Auth., 1 USPQ2d 1337, 1341 (Fed. Cir. 1986). "There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." Scripps Clinic v. Genentech Inc., 18 USPQ2d 1001, 1010 (Fed. Cir. 1991) (citations omitted).

The Examiner has rejected claims 1-3, 8, 13-15, 17, 18, 23 and 24 under 35 U.S.C. § 102(b) as being anticipated by Keana *et al.*, U.S. Pat. No. 5,580,697. The Examiner reasons that Keana *et al.* disclose methods for covalently modifying surfaces of various substrates. The Examiner notes that the surfaces are exposed to a reagent, having molecules each comprising a nitrenogenic group and a fuctionalizing group, in the presence of energized particles or heat, which transform the nitrenogenic reagent to a nitrene intermediate. The nitrene intermediate covalently reacts with any of various chemical groups present on the substrate surface, such as -CH, -NH, -OH, -C=C-, -C-C- and other groups on the substrate surface, so as to cause "nitrene addition" or "nitrene insertion" of the functionalizing reagent to the substrate surface. Nitrenes can undergo addition at -C-C- and -C=C- bonds to form a ring which the Examiner provides can be viewed as a [1+2] cycloaddition reaction or ene reaction.

The Examiner further provides that the functionalizing reagent is preferably selected from the group consisting generally of aryl azides, alkyl azides, alkenyl azides, alkynyl azides, acyl azides and azidoacetyl derivatives. The azide may contain a variety of functional groups including maleimido groups or other dienophile groups which may serve as a dienophile in a Diels Alder cycloaddition reaction with a 1,3-diene containing molecule such as ergosterol. From this analysis the Examiner concludes that the teachings of Keana *et al.* anticipate claims 1-3, 8, 13-15, 17, 18, 23 and 24 of the instant invention. Applicant respectfully traverses this rejection.

The instant invention describes a method for immobilizing a molecule on a support. The fundamental aspect of this invention is the use of cycloaddition reactions, including but not limited to, Diels-Alder reactions, 1,3-dipolar cycloaddition reactions and [2+2] cycloaddition reactions, for the chemoselective immobilization of molecules on a support. According to the general method of the present invention as set forth in claim 1, the molecule to be immobilized is first derivatized with a moiety capable of undergoing a cycloaddition reaction, followed by reaction with a support which has been derivatized with a moiety capable of undergoing reaction with the derivatized molecule of interest to yield, via a cycloaddition reaction, efficient immobilization of the molecule to the support. Thus, with reference to the scheme below, an oligonucleotide to be immobilized is functionalized with a diene to provide the derivatized oligonucleotide **23**, which is then immobilized on a solid support by Diels-Alder (DA) reaction with a maleimide funtionalized support, such as a maleimide functionalized glass slide. (Specification, Example 9, pages 42-44).

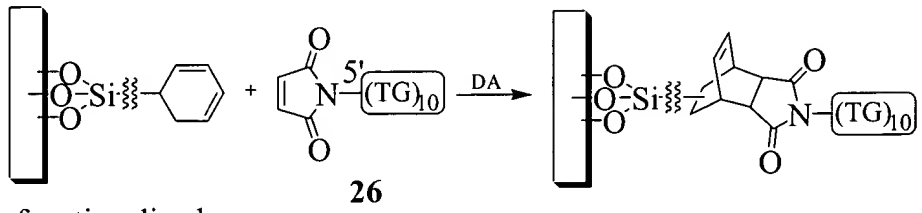


23

maleimide functionalized glass slide

In the alternative, the oligonucleotide to be immobilized is functionalized with a dienophile to provide the derivatized oligonucleotide **26**, which is then immobilized on a solid support by Diels-Alder (DA) reaction with a solid support which has been derivatized with a

diene, such as the diene derivatized glass slide illustrated in the following scheme. (Specification, Example 11, pages 47-48).

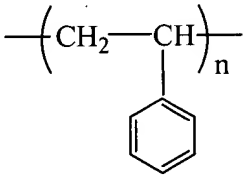


26

diene functionalized glass slide

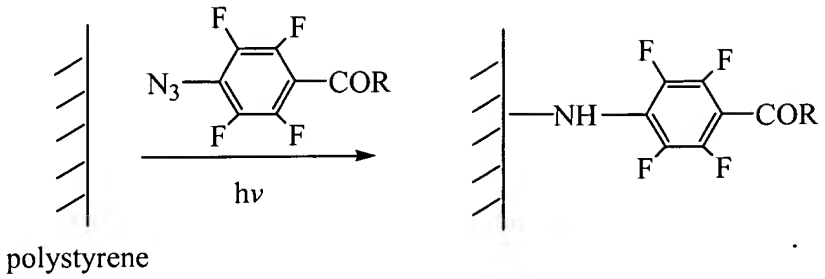
Thus, a key stem in the method of the present invention as described and claimed is the appropriate derivatization of the molecule to be immobilized.

Keana *et al.* describe a method for covalently modifying the surface of various substrates, including polymeric, siliceous, metallic allotrophic forms of carbon and semiconductor surfaces. According to the method of Keana *et al.*, substrate surfaces are functionalized by exposing the surface to a nitrenogenic functionalizing reagent in the presence of an energy source such as heat or light. The functionalizing reagent forms a nitrene intermediate which then covalently reacts with various groups on the surface of the substrate. In order to form nitrene intermediates, the functionalizing reagent used for reaction with the surface molecules must terminate with an azide or other analogous group. (Keana *et al.*, col. 2, lines 36-51). As explained in the Keana *et al.* reference nitrenes are highly reactive species that can react in a number of ways including insertion at CH and NH sites and addition at C-C and C=C bonds. In all of the examples provided in the Keana *et al.* reference, the nitrene generated reacts with a polymer surface by insertion into a CH bond at the surface of the polymer. Thus, with reference to Example 1 (Keana *et al.*, Specification, col. 15), the surface of polystyrene which has the following structure:



polystyrene

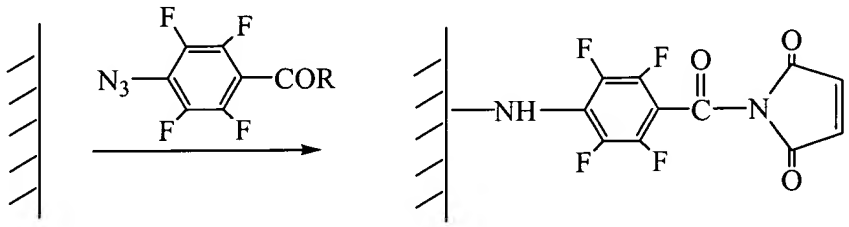
is functionalized via a nitrene insertion reaction with a perfluorophenyl azide reagent as illustrated in the following scheme:



polystyrene

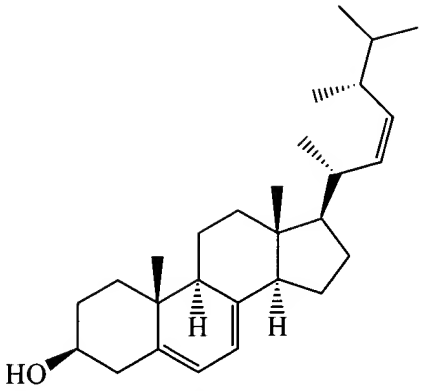
Keana *et al.* provide no example of surface functionalization via a cycloaddition reaction, rather the reference merely provides that nitrenes are known to react with double bonds to form aziridines. (Keana *et al.* Specification, col. 5, lines 36-40).

As noted above, nitrenes are highly reactive intermediates, thus it is not at all certain that the nitrene addition reaction described, but not illustrated by means of an actual example by Keana *et al.*, could in fact be selectively performed using highly functionalized molecules. As is well known, one of the challenges of synthetic chemistry is to determine the conditions under which known reactions can be performed in specific situations. Further, Keana *et al.* provide no examples of the synthesis of derivatized molecules, such as derivatized oligonucleotides, which are the required starting materials for the method of the instant invention. Thus, Keana *et al.* use a reactive nitrene generated from an azide to perform the functionalization/conjugation of the solid support (A) as illustrated by the following scheme:



polystyrene R=maleimido A

which they then provide can theoretically react with a 1,3-diene-containing molecule, such as ergosterol which has the following structure:



ergosterol

Keana *et al.*, however do not provide an actual example of such a reaction, nor does Keana *et al.* provide an example of the derivatization of the molecule to be immobilized. In the case of ergosterol, the reactant already contains a 1,3-diene and thus does not have to be functionalized prior to reaction with the derivatized support. Thus, upon immobilization the chemical and biological properties of ergosterol are substantially altered, whereas in the instant case these properties would remain essentially unchanged.

As provided above, Section 102 requires the presence in a single prior art reference of each and every element of the claimed invention. In the instant case, Keana *et al.* does not teach the derivatization and subsequent immobilization of a molecule via a cycloaddition reaction. In both inventions a molecule gets linked to a solid support, however Keana *et al.* accomplish this using a nitrene insertion reaction, whereas in the present invention a cycloaddition approach is used. Therefore, for the reasons discussed above Applicant respectfully requests that this rejection be withdrawn.

Applicant believes that the pending claims are now in condition for allowance. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 19-5117 if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to deposit account No. 19-5117.

Respectfully submitted,

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